

7/15/04

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NEWS 6 May 27 CAplus super roles and document types searchable in REGISTRY
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NEWS 10 Jul 12 BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS

NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0C(ENG) AND V6.0JC(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004

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FILE 'HOME' ENTERED AT 14:58:29 ON 15 JUL 2004

=> file registry
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL
ENTRY SESSION
0.21 0.21

FILE 'REGISTRY' ENTERED AT 14:58:37 ON 15 JUL 2004
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10656934

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STRUCTURE FILE UPDATES: 13 JUL 2004 HIGHEST RN 709042-93-3
DICTIONARY FILE UPDATES: 13 JUL 2004 HIGHEST RN 709042-93-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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<http://www.cas.org/ONLINE/DBSS/registryss.html>

| => file registry | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| COST IN U.S. DOLLARS | | |
| FULL ESTIMATED COST | 1.26 | 1.47 |

FILE 'REGISTRY' ENTERED AT 15:00:15 ON 15 JUL 2004
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STRUCTURE FILE UPDATES: 13 JUL 2004 HIGHEST RN 709042-93-3
DICTIONARY FILE UPDATES: 13 JUL 2004 HIGHEST RN 709042-93-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

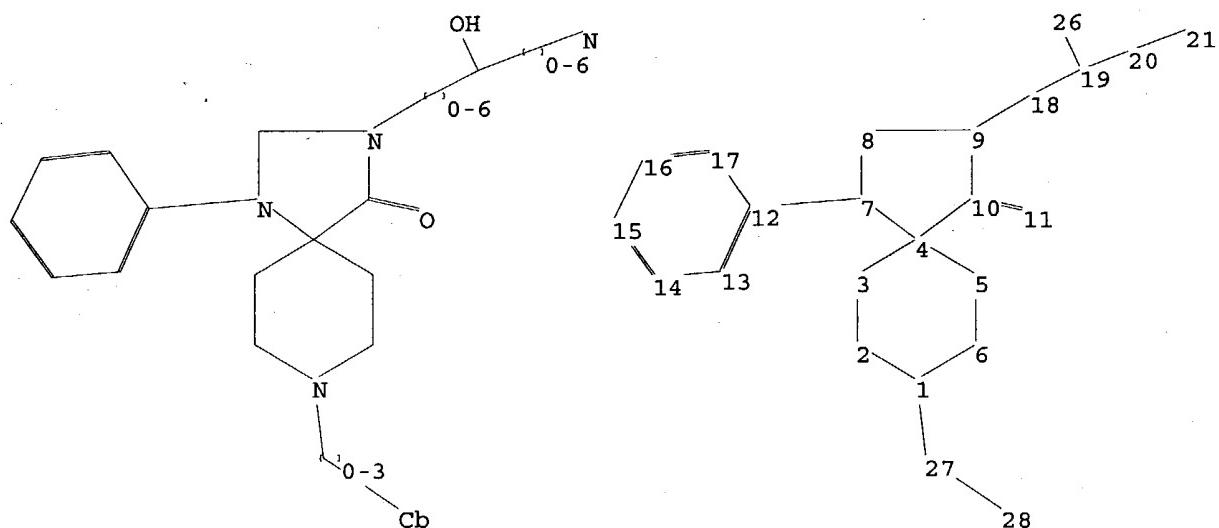
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:

<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>
Uploading C:\Stnexp4 corrupted\QUERIES\10656934.str

10656934

7/15/04



chain nodes :

11 18 19 20 21 26 27 28

ring nodes :

1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17

chain bonds :

1-27 7-12 9-18 10-11 18-19 19-20 19-26 20-21 27-28

ring bonds :

1-2 1-6 2-3 3-4 4-5 4-7 4-10 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17

exact/norm bonds :

1-2 1-6 1-27 2-3 3-4 4-5 4-7 4-10 5-6 7-8 7-12 8-9 9-10 9-18 10-11
19-26 20-21

exact bonds :

18-19 19-20 27-28

normalized bonds :

12-13 12-17 13-14 14-15 15-16 16-17

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 26:CLASS 27:CLASS 28:Atom

L1 STRUCTURE UPLOADED

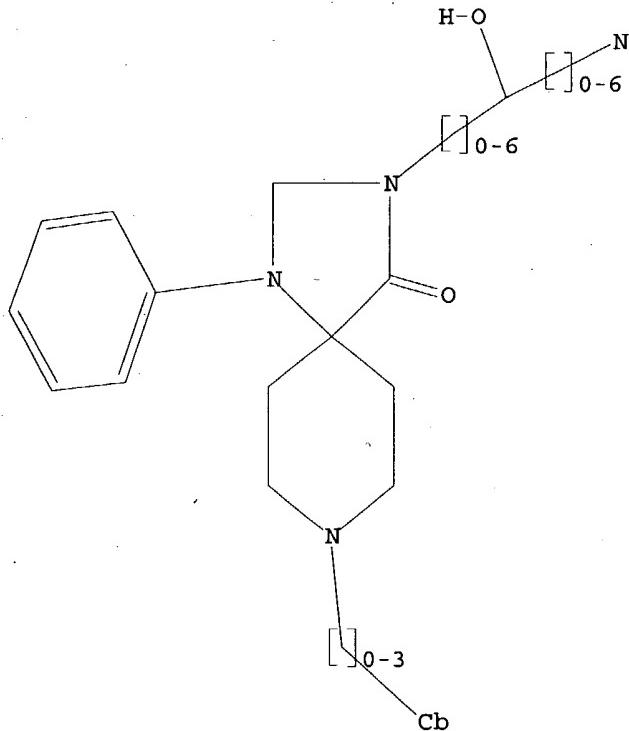
=> d 11

L1 HAS NO ANSWERS

L1 STR

10656934

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Structure attributes must be viewed using STN Express query preparation.

=> s 11
SAMPLE SEARCH INITIATED 15:00:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 33 TO ITERATE

100.0% PROCESSED 33 ITERATIONS 20 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 316 TO 1004
PROJECTED ANSWERS: 132 TO 668

L2 20 SEA SSS SAM L1

=> s 11 ful
FULL SEARCH INITIATED 15:00:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 875 TO ITERATE

100.0% PROCESSED 875 ITERATIONS 459 ANSWERS
SEARCH TIME: 00.00.01

L3 459 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
155.42 156.89

10656934

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FILE 'CAPLUS' ENTERED AT 15:00:48 ON 15 JUL 2004
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FILE COVERS 1907 - 15 Jul 2004 VOL 141 ISS 3
FILE LAST UPDATED: 14 Jul 2004 (20040714/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 13 L3

=> d abs bib fhitstr 1-13

7/15/04

L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R₀ = CRArbCOHra-(CRcRd)1-3X, (CRcRd)1-3COHraCraRbX; Ra, Rb = H, alkyl; Rc, Rd = H, OH, carboxy, etc.; X = NR1R2, CONR1R2, NR1, etc.; R1, R2 = H, alkyl, alkoxy, etc.; R3 = aryl, arylalkyl, heteroaryl, etc.; A = (R4)n; R4 = OH, alkyl, alkyl-OH; n = 0-2; B = (L1)m; L1 = alkyl,

alkenyl with provisos; m = 0-1; C = (R5)p and (R6)q substituted cycloalkyl, partially unsatd. carbocyclc (sic), aryl, etc.; R5 = OH, carboxy, halo, etc.; p = 0-5; R6 = (L2)10-1R7; q = 0-1; L2 = alkyl, alkenyl, alkynyl, etc.; R7 = aryl, partially unsatd. carbocyclc, cycloalkyl, etc.] and their pharmaceutically acceptable salts were prepared.

For example, amination of epoxide II, e.g., prepared from cyclooctanecarboxaldehyde in 2-steps, with 4-aminopyridine afforded amino alc. III. In human ORL-1 receptor binding affinity assays, approx. 470-examples of compds. I exhibited IC₅₀ values ranging from 0.10 - >10,000 nM, e.g., the IC₅₀ value of triazaspiro[4.5]decan-4-one III was 8.73 nM. Compds. I are claimed useful for the treatment of anxiety, depression, migraine, etc..

AN 2004:20333 CAPLUS

DN 140:270854

TI Preparation of 1,3,8-triazaspiro[4.5]decan-4-ones for the treatment of ORL-1 receptor mediated disorders

IN Battista, Kathleen; Bignan, Gilles; Connolly, Peter J.; Reitz, Allen B.; Morgan Ross, Tina; Scott, Malcolm; Middleton, Steve A.; Orsini, Michael

PA Janssen Pharmaceutica, N.V., Beig.

SO PCT Int. Appl., 249 pp.

CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

PI WO 2004022558 A2 20040318 WO 2003-US27956 20030905

WO 2004022558 A3 20040521

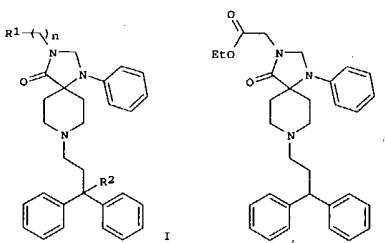
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PRAI US 2002-409134P P 20020909

OS MARPAT 140:270854

IT 674456-04-3P

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI



AB Title compds. I are disclosed [(a): R₁ = H, COOH, COOR₃, CONH₂ or (di)alkyl derivs., cyano, NH₂O-alkyl, or 1H-tetrazol-5-yl; R₂ = COOH, COOR₃, or (CH₂)_m-1H-tetrazol-5-yl; R₃ = alkyl, PhCH₂, Ph, or cycloalkyl, n = 0 when R₁ = H, and n = 1-4 when R₁ = H; m = 0-4; or (b): R₁ = as above except H; R₂ = COOH, COOR₃, CONH₂ or (CH₂)_m-1H-tetrazol-5-yl; R₃ = as above; n = 1-4; m = 0-4; or (c): R₁ = COOH, CONH₂ or (di)alkyl derivs.,

NH₂O-alkyl, or 1H-tetrazol-5-yl; R₂ = H; n = 1-4; including pharmaceutically acceptable salts]. Also disclosed are methods for treating or preventing pain in animals, comprising administration of I, and methods for stimulating opioid-receptor function in cells expressing opioid receptors, using I. Approx. 25 specific compds. I were prepared and/or claimed individually. For instance, 8-(3,3-diphenylpropyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one N-alkylated with ICH₂CO₂Et using NaH in DMF to give 74.7% invention compound II. In expts. using, e.g., recombinant HEK-293 cells expressing human opioid ORL-1 receptors, I₁ bound to μ -opioid receptors with a binding constant K_i of 2.9 nM, and ORL-1 receptors with a K_i of 18 nM. II stimulated μ -opioid receptor function, and exhibited a μ -GTP EC₅₀ of 44 nM and a μ -GTP Emax of 88%. II also stimulated ORL-1 opioid receptor function, and exhibited an ORL-1 GTP EC₅₀ of 71 nM and an ORL-1 GTP Emax of 95%.

AN 2003:972047 CAPLUS

DN 140:16729

TI Triazaspiro compounds, particularly

8-(3,3-diphenylpropyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one derivatives, with opioid receptor

stimulating

activity, useful for treating or preventing pain

IN Chen, Zhengming; Victory, Sam F.

PA Euro-Celtique, S.A., Luxembourg

SO PCT Int. Appl., 81 pp.

10656934

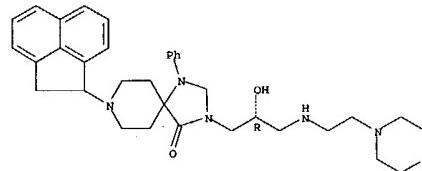
L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Uses)

(drug target; prepn. of triazaspiro[4.5]decan-4-one for the treatment of ORL-1 receptor mediated disorders)

RN 674456-04-3 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decan-4-one, 8-(1,2-dihydro-1-acenaphthylene)-3-((2R)-2-hydroxy-3-[(2-(4-morpholinyl)ethyl)amino]propyl)-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

PI WO 2003101953 A2 20031211 WO 2003-US17419 20030602

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MM, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, US, US, UZ, VA, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-384007P P 20020531

US 2003-460219P P 20030403

US 2003-448627 A 20030529

OS MARPAT 140:16729

IT 630425-71-7P, 2-[B-(3,3-Diphenylpropyl)-4-oxo-1-phenyl-1,3,8-

triazaspiro[4.5]decan-3-yl]acetamide

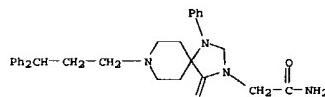
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses)

(drug candidate; preparation of triazaspiro compds. as opioid receptor stimulants useful for treating or preventing pain)

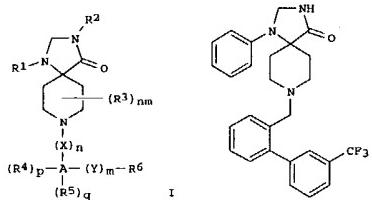
PN 630425-71-7 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 8-(3,3-diphenylpropyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



7/15/04

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
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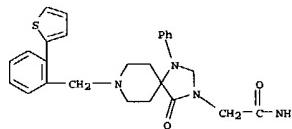


- AB** The invention is directed to novel 1,3,8-triazaspiro[4.5]decan-4-one derive. of general formula I, useful in the treatment of disorders and conditions mediated by the ORL-1 G-protein coupled receptor (wherein: R1 = H, alkyl, (un)substituted aryl or aralkyl; R2 = H, alkenyl, alkynyl, (un)substituted alkyl, aryl, cycloalkyl, partially unsatd. carbocyclyl, heterocarlyl; nm = 0-2; R3 = alkyl or hydroxylalkyl; n = 0-1; X = alkenyl, (un)substituted alkyl, alkyl-O, or alkyl-S (alkyl attached to spiro ring atom); A = Ph or 5- or 6-membered heteroaryl nucleus; p = 0-1; R4 = aryl, cycloalkyl, partially unsatd. carbocyclyl, heteroaryl, heterocycloalkyl; q = 0-3; R5 = halo, alkyl, haloalkyl, alkoxy, NO₂, (di)(alkyl)amino, alkylsulfonyl, (di)(alkyl)amido, sulfonyl, (di)(alkyl)aminosulfonyl; m = 0-1; Y = alkyl, alkenyl, O, S, NH, N-(alkyl), alkyl-O, alkyl-S, O-alkyl, S-alkyl-S; R6 = (un)substituted aryl, partially unsatd. carbocyclyl, cycloalkyl, heteroaryl, or heterocycloalkyl, or benzoyloxyphenyl; with provisos: including pharmaceutically acceptable salts). More particularly, the compds. of the invention are useful in the treatment of disorders and conditions such as anxiety, depression, substance abuse, neuropathic pain, acute pain, migraine, asthma, and cough, and also for improving cognition. Over 130 examples were individually prepared and tested. For instance, 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one was N-alkylated with 2-bromobenzyl bromide, and the resultant aryl bromide was coupled with 3-(trifluoromethyl)phenylboronic acid under Pd(PPh₃)₄ catalysis, to give title compound II. In a test for inhibition of binding of 125I-Tyr14-nociceptin to human nociceptin receptors (ORL-1) expressed on HEK293 cell membranes, I had IC₅₀ values from 0.0010 μM to >10 μM.
- AN** 2002:814132 CAPLUS
DN 137:325418
TI 1,3,8-Triazaspiro[4.5]decan-4-one derivatives useful for the treatment of

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

- IN** Jordan, Alfonzo; Pan, Kevin; Reitz, Allen B.
PA Ortho-McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
PAN.CNT 1
- | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2002083673 | A1 | 20021024 | WO 2002-US10736 | 20020405 |
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| US 2003109539 | | | | |
| US 2003109539 A1 20030612 US 2002-117674 20020405 | | | | |
| EP 1392687 A1 20040303 EP 2002-721678 20020405 | | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRAI US 2001-282722P P 20010410 | | | | |
| WO 2002-US10736 W 20020405 | | | | |
| OS MARPAT 137:325418 | | | | |
| IT 473528-08-4 CAPLUS | | | | |
| CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 4-oxo-1-phenyl-8-[(2-(2-thienyl)phenyl)methyl]-1,3,8-triazaspiro[4.5]decan-3-acetamide | | | | |
| RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); drug candidate; preparation of triazaspirodecanone derivs. for treatment of ORL-1 receptor-mediated disorders) | | | | |
| RN 473528-08-4 CAPLUS | | | | |
| CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 4-oxo-1-phenyl-8-[(2-(2-thienyl)phenyl)methyl]- (9CI) (CA INDEX NAME) | | | | |



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

- AB** The "one-bead one-compound" (OBOC) combinatorial library method is highly efficient, especially when used with well-established on-bead binding or functional assays. Literally, millions of compds. can be screened concurrently within 1 to 2 days. However, structure determination of peptidomimetic and small mol. compds. on one single bead is not trivial. A novel, highly efficient, and robust peptide-based encoding system has been developed for OBOC peptidomimetic and small mol. combinatorial libraries. In this system, topol. segregated bifunctional beads, which are made by a simple biphasic solvent strategy, are employed for the preparation and screening of an OBOC combinatorial peptidomimetic and small mol. libraries. Testing mols. are on the outer layer, and the coding tags in the interior of the bead do not interfere with screening. The coding tag is a peptide containing a large number of unnatural α-amino acids derived from different building blocks used for generating the peptidomimetic or small mol. By coupling common building blocks simultaneously to the scaffold of the testing compound and to the side chains of the α-amino acids on the coding peptide, extra synthetic steps are eliminated and the amount of undesirable side products is minimized. Pos. bead decoding is easy and straightforward as there is no need for cleavage and retrieval of the coding tag, and pos. beads can be sequenced directly with Edman degradation. The authors demonstrate the efficiency and simplicity of their peptidyl encoding system by generating an encoded 158 400-member model peptidomimetic library and screening it for ligands that bind to streptavidin. Potent and novel ligands with clear motifs have been identified.

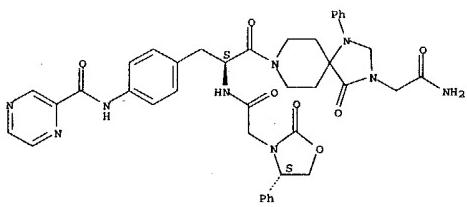
- AN** 2002:424638 CAPLUS
DN 137:140770
TI A Novel Peptide-Based Encoding System for "One-Bead One-Compound" Peptidomimetic and Small Molecule Combinatorial Libraries
AU Liu, Ruwei; Marik, Jan; Lam, Kit S.
CS Division of Hematology & Oncology Department of Internal Medicine, UC Davis Cancer Center University of California Davis, Sacramento, CA, 95817, USA
SO Journal of the American Chemical Society (2002), 124(26), 7678-7680 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
IT 444794-81-4# RL: BSU (Biological study, unclassified); CPN (Combinatorial preparation); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation) (solid-phase preparation of a library of biol. active peptides using the "one-bead one-compound" combinatorial method, a novel peptide-based encoding system and a streptavidin-binding assay)
RN 444794-81-4 CAPLUS
CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 4-oxo-8-[(2S)-1-oxo-2-[[[(4S)-2-oxo-4-phenyl-3-oxazolidinyl]acetyl]amino]-3-[4-(pyrazinylcarbonyl)amino]phenyl]propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10656934

7/15/04

L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compd. I [R1 = H, alkyl, alkenyl, Ph, (CH2)m-non aromatic heterocyclyl, (CH2)m-heteroaryl, (CH2)m-carboxamide, (CH2)m-C(O)alkyl, etc.; R2 = H, alkyl, halo, alkoxy; R3 = alkyl, alkoxy, halo, CR3; X = N-, alkyl, (CH2)m-Ph or may be together an oxo group; Y1/Y2 = H, alkyl, (CH2)m-Ph or may be together an oxo group; Z = bond, CH2, C(O); m = O - 4; n = 2 - 3; p = 0 - 2] were prepared Over 160 synthetic examples were disclosed. For example,

8-(3,5-bis(trifluoromethylbenzoyl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one was reacted with 2-chloro-4,6-dimethoxyethane, NaH, 100°C, 1 h to give II. II had pKi = 8.66 for the NK-1 receptor. I are useful in the treatment of diseases related to NK-1 receptor antagonists.

AN 2001:904170 CAPLUS

DN 136:37519

TI Synthesis and use of triazaspirodecanone derivatives as neurokinin receptor antagonists

IN Gallez, Guido; Godet, Thierry; Goergler, Annick; Hoffmann, Torsten; Kolczewski, Sabine; Roever, Stephan

PA P. Hoffmann-La Roche AG, Switz.

SO PCT Int. Appl., 90 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|----------------|----------|-----------------|------|
| PI WO 2001094346 A1 20011213 | WO 2001-EP6305 | 20010601 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, NC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002006932 A1 20020117 | US 2001-861795 | 20010521 | | |
| US 6482829 B2 20021119 | | | | |
| EP 1392596 A1 20030319 | EP 2001-945242 | 20010601 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2001011538 A 20030701 | BR 2001-11538 | 20010601 | | |
| JP 2003535863 T2 20031202 | JP 2002-501895 | 20010601 | | |
| PRAI EP 2000-112285 A 20000608 | | | | |
| WO 2001-EP6305 W 20010601 | | | | |

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

OS MARPAT 136:37519

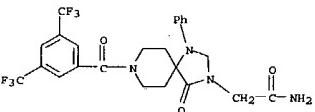
IT 380198-55-09

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis and use of triazaspirodecanone derivs. as neurokinin receptor antagonists)

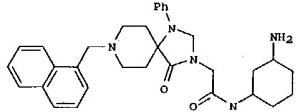
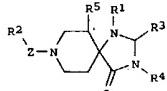
RN 380198-55-0 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 8-[1,5-bis(trifluoromethyl)benzoyl]-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI



AB The title compds. [I; R1 = (un)substituted Ph, aralkyl, thieryl, etc.; R2 = aminophenyl, cyanophenyl, alkylphenyl, etc.; R3 = H, alkyl, Ph, etc.; R4 = (CH2)mNR9(CH2)nR8 (m = 1-8; n = 0-8; A = CH2, CO; R8 = NR11R12, etc.; R9 = H, alkyl, etc.; R11, R12 = H, aminoalkyl); R5 = H, alkyl; Z = CHR10 (R10 = H, alkyl, etc.), alkylene, alkenylene, etc.] and their pharmaceutically acceptable salts which have high affinity for nociceptin receptors, and are useful for the treatment of migraine, non insulin dependent diabetes mellitus (type II diabetes), sepsis, inflammation, incontinence and/or vasomotor disturbances, in particular the peripheral vasoconstrictor effects known as hot flushes or hot flashes, were prepared and formulated. E.g., a solid phase synthesis of cis/trans-II,2R3CO2H was given. The compds. I are effective at 10-100 mg/day/patient.

AN 2001:380584 CAPLUS

DN 135:5615

TI Preparation of novel triazaspirodecanones with high affinity for opioid receptor subtypes

IN Hohweg, Rolf; Watson, Brett; Pettersson, Ingrid

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------------|----------|-----------------|------|
| PI WO 2001036418 A1 20010525 | WO 2000-DK41 | 20001117 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GH, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU | | | | |

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7/15/04

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, PI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI DK 1999-1653 A 19991117
 US 1999-167019P P 19991129

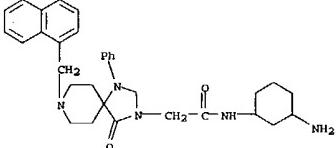
OS MARPAT 135:5615

IT 340804-62-8P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of novel triazaspirodecanones with high affinity for
 opioid receptor subtypes)

RN 340804-62-8 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(3-aminocyclohexyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RW: GH, GM, KE, LS, MW, SD, SL, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, PI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6262066 B1 20010717 US 1999-359771 19990726

EP 1200087 A1 20020502 EP 2000-904560 20000126

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL

BR 2000012801 A 20020507 BR 2000-12801 20000126

JP 2003505420 T2 20030212 JP 2001-511934 2000126

US 2001011092 A1 20010802 US 2001-769824 20010125

US 6455527 B2 20020924

ZA 2002-00275 A 20030411 ZA 2002-275 20020111

NO 2002000392 A 20020325 NO 2002-392 20020125

US 2003073690 A1 20030417 US 2002-155277 20020523

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PRAI US 1999-359771 A 19990726

US 1998-94240P P 19980727

US 2000-491780 A1 20000126

WO 2000-US1853 W 20000126

US 2001-769824 A3 20010125

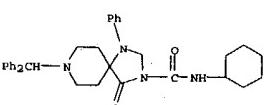
OS MARPAT 134:131434

IT 256940-47-3P

RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of substituted piperidines as nociceptin receptor ORL-1
 agonists for use in treating cough)

RN 256940-47-3 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decane-3-carboxamide, N-cyclohexyl-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



• HCl

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

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AB The title compds. [I]: X1 = (un)substituted alkyl, cycloalkyl, aryl, etc.; X2 = CHO, CN, (un)substituted NH2, etc.; or X1 = (un)substituted benzofused heterocycl and X2 = H; or X1 and X2 together form an optionally benzofused spiro heterocycl group; R1-R4 = H, alkyl; or (R1 and R4) or (R2 and R3) or (R1 and R3) or (R2 and R4) together can form an alkenylene bridge; Z1 = (un)substituted alkyl, aryl, heteroaryl, etc.; Z2 = H, Z1; Z3 = H, alkyl; or Z1-Z3, together with the carbon to which they are attached, form bicyclic saturated or unsatd. ring(s) and their pharmaceutically acceptable salts, useful as ORL-1 receptor agonists for the treatment of cough, alone or in combination with one or more agents for the treatment of cough, allergy or asthma symptoms, were prepared and formulated. Thus,

reacting 4-hydroxy-4-phenylpiperidine with α -bromodiphenylmethane in the presence of CuClO₂ in CH₃CN afforded 90% II which showed Ki of 13 nM against ORL-1 receptor binding.

AN 2001-78241 CAPLUS

DN 134:131434

TI Preparation of substituted piperidines as nociceptin receptor ORL-1 agonists for use in treating cough

IN Tulshian, Deen; Ho, Ginny D.; Silverman, Lisa S.; Matasi, Julius J.; McLeod, Robbie L.; Hey, John A.; Chapman, Richard W.; Bercovici, Ana; Cuss, Francis M.

PA Schering Corporation, USA

SO PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DT Patent

LA English

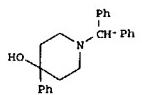
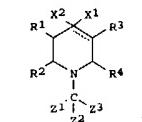
FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2001007050 A1 20010201 WO 2000-US1853 20000126
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ,
 DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP,
 KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO,
 NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
 UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

GI



AB Compds. of formula I [wherein: the dotted line represents an optional double bond; X1 = (un)substituted alkyl, cycloalkyl, aryl, heteroaryl or heterocycloalkyl; X2 = CHO, CN, optionally substituted amino, alkyl, or aryl; or X1 = (un)substituted benzofused heterocycl and X2 = H; or X1 and X2 together form an optionally benzofused spiro heterocycl group; R1, R2, R3 and R4 = independently H and alkyl, or (R1 and R4) or (R2 and R3) or (R1 and R3) or (R2 and R4) together can form an alkenylene bridge of 1

and X2 together form an optionally benzofused spiro heterocycl group; R1, R2, R3 and R4 = independently H and alkyl, or (R1 and R4) or (R2 and R3) or (R1 and R3) or (R2 and R4) together can form an alkenylene bridge of 1 to

3 carbon atoms; Z1 = (un)substituted alkyl, aryl, heteroaryl, cycloalkyl or heterocycloalkyl, or CO₂(alkyl or substituted amino) or CN; Z2 = H or Z1; Z3 = H or alkyl; or Z1, Z2 and Z3, together with the carbon to which they are attached, form bicyclic saturated or unsatd. ring(s) or pharmaceutically acceptable salt or solvate thereof useful as nociceptin receptor inhibitors for the treatment of pain, anxiety, cough, asthma, depression, and alc. abuse are disclosed. Compound II showed the Ki value

of 13 nM in an in vitro test for ORL-1 receptor binding assay. Formulations are given.

AN 2000-98519 CAPLUS

DN 132:137290

TI Preparation of piperidine derivatives as high affinity ligands for nociceptin receptor ORL-1

IN Tulshian, Deen; Ho, Ginny D.; Silverman, Lisa S.; Matasi, Julius J.; McLeod, Robbie L.; Hey, John A.; Chapman, Richard W.; Bercovici, Ana; Cuss, Francis M.

PA Schering Corporation, USA

SO PCT Int. Appl., 88 pp.

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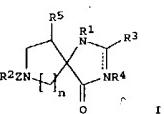
7/15/04

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CODEN: PIXKD2
 DT Patent
 LA English
 PAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|----------------------------|----------|
| PI WO 2000006545 | A1 | 20000210 | WO 1999-US14165 | 19990726 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TM, TR, TT, UA, UZ, VN, YU, ZA,
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2338206 | AA | 20000210 | CA 1999-2338206 | 19990726 |
| AU 9952056 | A1 | 20000221 | AU 1999-52056 | 19990726 |
| AU 768607 | B2 | 20031218 | | |
| BR 9912495 | A | 20010502 | BR 1999-12495 | 19990726 |
| EP 1100781 | A1 | 20010523 | EP 1999-937174 | 19990726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO | | | | |
| TR 200100241 | T2 | 20010621 | TR 2001-200100241119990726 | |
| JP 2002521472 | T2 | 20020716 | JP 2000-562351 | 19990726 |
| TW 502021 | B | 20030911 | TW 1999-88112624 | 19990726 |
| EP 1258244 | A1 | 20021120 | EP 2002-18161 | 19990726 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY | | | | |
| NZ 509033 | A | 20031128 | NZ 1999-509033 | 19990726 |
| ZA 200100150 | A | 20020107 | ZA 2001-150 | 20010105 |
| NO 2001000467 | A | 20010326 | NO 2001-467 | 20010126 |
| PRAI US 1998-122878 | A | 19980727 | | |
| EP 1999-937174 | A3 | 19990726 | | |
| WO 1999-US14165 | W | 19990726 | | |
| OS MARPAT 132:137290 | | | | |
| IT 256940-47-3P | | | | |
| RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine derivs. as high affinity ligands for nociceptin receptor ORL-1)
RN 256940-47-3 CAPLUS
CN 1,3,8-Triazaspiro[4.5]decane-3-carboxamide, N-cyclohexyl-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME) | | | | |

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
 GI



AB The title triazaspiro compds. I [R1 = Ph, arylalkyl or thienvl; R2 = aminophenyl, C1-6-monoalkylaminophenyl, C1-6-dialkylaminophenyl, cyanophenyl, C2-6-alkylphenyl, naphthyl, tetrahydronaphthyl, furanyl, indanyl, KF, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, acting as opioid receptor ligands for the treatment of vasomotor disturbances (no data), were prepared. E.g., (4-oxo-8-phenethyl-1-phenyl-1,3,8-triazaspiro[4.5]decane-3-yl)acetic acid Me ester was prepared.

AN 1999-753237 CAPLUS

DN 132:3310

TI Preparation of novel 1,3,8-triazaspiro[4.5]decanones with high affinity for opioid receptor subtypes

IN Watson, Brett; Hohlweg, Rolf; Thomsen, Christian

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 93 pp.

CODEN: PIXKD2

DT Patent

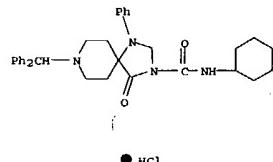
LA English

PAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 995997 | A1 | 19991125 | WO 1999-DK266 | 19990514 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CP, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6277951 | B1 | 20010821 | US 1999-311469 | 19990513 |
| AU 9538059 | A1 | 19991206 | AU 1999-38099 | 19990514 |
| EP 1080091 | A1 | 20010307 | EP 1999-920561 | 19990514 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2002515503 | T2 | 20020528 | JP 2000-549615 | 19990514 |
| PRAI DN 1998-681 | A | 19980518 | | |
| DK 1998-711 | A | 19980520 | | |
| DK 1998-729 | A | 19980526 | | |

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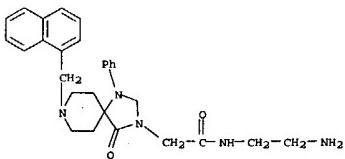
L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

| | | |
|---|---|----------|
| DK 1998-927 | A | 19980710 |
| DK 1999-111 | A | 19990129 |
| US 1998-91012P | P | 19980626 |
| US 1998-93519P | P | 19980721 |
| US 1999-120295P | P | 19990216 |
| WO 1999-DK266 | W | 19990514 |
| MARPAT 132:3310 | | |
| IT 256946-42-1P | | |
| RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 1,3,8-triazaspiro[4.5]decanones and their affinity for opioid receptor subtypes) | | |
| RN 256946-42-1 CAPLUS | | |
| CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(2-aminoethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, dihydrochloride (9CI) (CA INDEX NAME) | | |

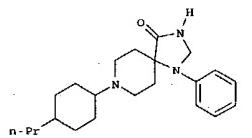
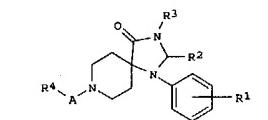


● 2 HCl

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

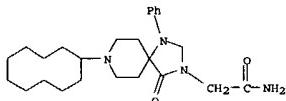
7/15/04

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI



AB The invention relates to compds. I [wherein R1 = H, alkyl, halo, alkoxy, CF3, phenylalkyl, or C5-7 cycloalkyl; R2 = H, alkyl, Ph, or phenylalkyl; R3 = H, alkyl, PhCH2, phenylalkyl, diphenylalkyl, triazinyl, cyanomethyl, piperidinyllalkyl, naphthylalkyl, C5-7 cycloalkyl, C5-7 cycloalkylalkyl, pyridinylalkyl, morpholinylalkyl, dioxolanylalkyl, oxazolylalkyl, or 2-oxo-oxazolidinylalkyl [wherein ring systems may be substituted], or (CH2)nCO2-lower alkyl, (CH2)nCONH2, (CH2)nCON(lower alkyl)2, (CH2)nOH, or (CH2)nCONHCH2C6H5; R4 = H, alkyl, or nitrilo; A = various ring systems including (un)substituted cycloalkane, decalin, hex- or octa hydroindene, bicyclo[3.1.0]hexane, dodecahydrocyclophosphene-1-yl, bicyclo[6.2.0]dec-9-yl, and bicyclonan-9-yl] and their pharmaceutically acceptable acid addition salts. The compds. are agonists and/or antagonists of the Orphanin FQ (OFQ) receptor. Consequently, they will be useful in the treatment of memory and attention deficits, psychiatric, neurol. and physiol. disorders, especially, but not limited to, amelioration of symptoms of anxiety and stress disorders, depression, trauma, memory loss due to Alzheimer's disease or other dementias, epilepsy and convulsions, acute and/or chronic pain conditions, symptoms of addictive drug withdrawal, control of water balance, Na+ excretion, arterial blood pressure disorders and metabolic disorders such as obesity. Over 100 examples, mostly as HCl salts, were prepared. For instance, condensation of 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one with 4-propylcyclohexanone in refluxing PhMe, followed by reduction with

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



• HCl

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
NaBH3CN in THF/EtOH mixt., workup, chromatog., and crystn., gave title compd. II-HCl as a cis/trans mixt. The affinity of II-HCl for OFQ receptors (receptors expressed in transfected HEK-293 cells), given as

the pKi was 8.4.
AN 1999-375286 CAPLUS
DN 131-44826

TI 1,3,8-Triazaspiro[4.5]decan-4-one derivatives useful as OFQ receptor agonists and antagonists
IN Adam, Geo; Cesura, Andrea; Galley, Guido; Jenck, Francois; Rover, Stephan;

Wichmann, Jurgen
PA F. Hoffmann-La Roche A.-G., Switz.
SO Eur. Pat. Appl., 35 PP.

CODEN: EPXXDW

DT Patent

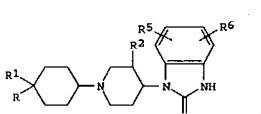
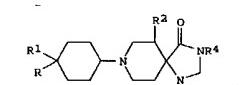
LA English

PAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| EP 921125 | A1 | 19990609 | EP 1998-122511 | 19981127 |
| EP 921125 | B1 | 20020130 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| AT 212635 | E | 20020215 | AT 1998-122511 | 19981127 |
| PT 921125 | | 20020628 | PT 1998-122511 | 19981127 |
| ES 2170446 | T3 | 20020801 | ES 1998-122511 | 19981127 |
| SG 71173 | A1 | 20000321 | SG 1998-5141 | 19981203 |
| US 6043366 | A | 20000328 | US 1998-204184 | 19981203 |
| NZ 333159 | A | 20000623 | NZ 1998-333159 | 19981203 |
| NO 9805684 | A | 19990607 | NO 1998-5684 | 19981204 |
| ZA 9811128 | A | 19990607 | ZA 1998-11128 | 19981204 |
| AU 9896087 | A1 | 19990624 | AU 1998-96087 | 19981204 |
| AU 744338 | B2 | 20020221 | | |
| CN 2225251 | A | 19990714 | CN 1998-122759 | 19981204 |
| CN 1118467 | B | 20030820 | | |
| JP 11228575 | A2 | 19990824 | JP 1998-345278 | 19981204 |
| JP 3366868 | B2 | 20030114 | | |
| BR 9805297 | A | 20000201 | BR 1998-5297 | 19981204 |
| TW 408123 | B | 20000101 | TW 1998-87120132 | 19981204 |

PRAI EP 1997-121427 A 19971205
OS MARPAT 131-44818
IT 227028-91-3P, 2-(8-Cyclodetyl-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-3-yl)acetamide hydrochloride
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses); (target compound; preparation of triazaaspirodecanone derivs. as OFQ receptor agonists and antagonists)
RN 227028-91-3 CAPLUS
CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, 8-cyclodetyl-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
GI



AB Arylcyclohexylpiperidines I and II [R = aryl, 1,3-benzodioxolyl; R1 = H, cyano, CO2H, esterified or amidated CO2H, OH, acyloxy, alkoxy, acyl, alkyl, cyclohexyl; R2 = H, alkyl; R3 = aryl; R4 = H, (un)substituted alkyl; R5, R6 = H, halogen, CF3, alkyl, alkoxy] were prepared. Thus II (R = 4-FCGH4, R1 = OH, R2 = R5 = R6 = H) was obtained by reductive amination of the cyclohexanone by the piperidinylbenzimidazolone. I and II have psychotropic and antiemetic activity.

AN 1982-492279 CAPLUS

DN 97-92279

TI 1-(4-Arylcyclohexyl)piperidine derivatives, their use and their pharmaceutical compositions

IN Stokroekx, Raymond A.; Willems, Joannes J. M.; Luyckx, Marcel G. M.

PA Janssen Pharmaceutica N. V., Belg.

SO U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 199,142, abandoned.

CODEN: USXXAM

DT Patent

LA English

PAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| US 4329353 | A | 19820511 | US 1981-222091 | 19810109 |
| CA 1161438 | A1 | 19840131 | CA 1981-372317 | 19810304 |
| AU 8168092 | A1 | 19810917 | AU 1981-68092 | 19810305 |
| AU 538147 | B2 | 19840802 | | |
| JP 56150086 | A2 | 19811120 | JP 1981-31393 | 19810306 |
| JP 02001834 | B4 | 19900112 | | |
| FI 8100727 | A | 19810911 | FI 1981-727 | 19810309 |
| FI 73428 | B | 19870630 | | |
| FI 73428 | C | 19871009 | | |
| DK 8101071 | A | 19810911 | DK 1981-1071 | 19810309 |
| NO 8100793 | A | 19810911 | NO 1981-793 | 19810309 |
| NO 159793 | B | 19881031 | | |
| NO 159793 | C | 19890208 | | |
| EP 35902 | A1 | 19810916 | EP 1981-300973 | 19810309 |
| EP 35902 | B1 | 19841031 | | |

R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE

7/15/04

L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

| | | | |
|------------|-------------|-----------------|----------|
| ZA 8101558 | A 19821027 | ZA 1981-1558 | 19810309 |
| RO 81938 | P 19830601 | RO 1981-103622 | 19810309 |
| HU 27689 | O 19831028 | HU 1981-581 | 19810309 |
| HU 187362 | B 19851228 | | |
| SU 1095878 | A3 19840530 | SU 1981-3254454 | 19810309 |
| IL 62320 | A1 19840629 | IL 1981-62320 | 19810309 |
| AT 10096 | E 19841115 | AT 1981-300973 | 19810309 |
| RO 85814 | P 19841125 | RO 1981-110666 | 19810309 |
| ES 500251 | A1 19821101 | ES 1981-500251 | 19810310 |
| PL 129642 | B1 19840531 | PL 1981-216046 | 19810310 |
| PL 130480 | B1 19840831 | PL 1981-230073 | 19810310 |
| CS 234044 | B2 19850314 | CS 1981-1743 | 19810310 |
| SU 1099845 | A3 19840623 | SU 1982-3409919 | 19820329 |

PRAI US 1980-128705
US 1980-199142
US 1981-222091
EP 1981-300973

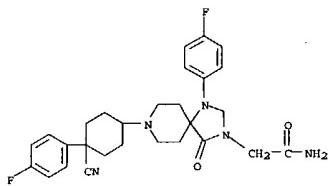
OS CASREACT 97:92279
IT 80913-19-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)

RN 80913-19-5 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-1-(4-fluorophenyl)-4-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

| | | | |
|---|-------------|-----------------|----------|
| PI EP 35902 | A1 19810916 | EP 1981-300973 | 19810309 |
| EP 35902 | B1 19841031 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | |
| US 4329353 | A 19820511 | US 1981-222091 | 19810109 |
| AU 8168092 | A1 19810917 | AU 1981-68092 | 19810305 |
| AU 538147 | B2 19840802 | | |
| ZA 8101558 | A 19821027 | ZA 1981-1558 | 19810309 |
| SU 1095878 | A3 19840530 | SU 1981-3254454 | 19810309 |
| AT 10096 | E 19841115 | AT 1981-300973 | 19810309 |
| SU 1099845 | A3 19840623 | SU 1982-3409919 | 19820329 |

PRAI US 1980-128705
US 1980-199142
US 1981-222091
EP 1981-300973

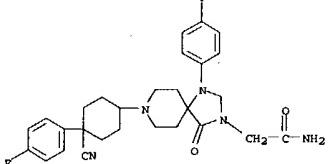
IT 80913-19-5P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and psychotropic and antiemetic activity of)

RN 80913-19-5 CAPLUS

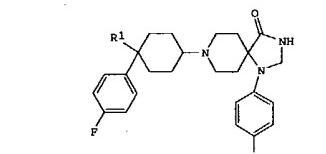
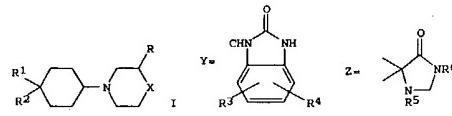
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-[4-cyano-4-(4-fluorophenyl)cyclohexyl]-1-(4-fluorophenyl)-4-oxo- (9CI) (CA INDEX NAME)



10656934

L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

GI



AB The antiemetic and psychotropic cyclohexylpiperidinylbenzimidazolones and cyclohexyltriazaspirodecanes I [R = H, alkyl; R1 = H, cyano, CO2H, carboxylic acid ester, (un)substituted aminocarbonyl, HO, alkoxy, alkylcarbonyloxy, HCO, acyl, arylcarbonyl, alkyl, alkenyl, alkynyl, cyclohexyl; R2 = aryl, 1,3-benzodioxolyl; X = Y (R3, R4 = H, halo, F, Cl, alkyl, alkoxy, Z (R5 = aryl, R6 = H, substituted alkyl) were prepared. Thus, Et 4-oxo-1-piperidinecarboxylate was treated with p-FC6H4NH2 and NaCN followed by hydrolysis and the resulting 4-carbamoyl-4-(4-fluorophenylamino)-1-piperidinecarboxylate was cyclized with paraformaldehyde to give Et 1-(4-fluorophenyl)-4-oxo-1,3,8-triazaspiro[4.5]decane-8-carboxylate, which underwent decarboethoxylation followed by treatment with 1-(4-fluorophenyl)-4-oxocyclohexanecarbonitrile to give the triazaspirodecano II (R1 = CN). The ED50 of II (R1 = CO2Et) in the apomorphine test in dogs was 2.5 mg/kg.

AN 1982-104237 CAPLUS

DN 96-104237

TI 1-(4-Aryl-cyclohexyl)piperidine derivatives

IN Stokbroekx, Raymond Antoine; Willems, Joannes Josephus Maria; Luyckx, Marcel Gerebernus Maria

PA Janssen Pharmaceutica N. V., Belg.

SO Eur. Pat. Appl., 62 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

GI For diagram(a), see printed CA Issue.

AB Neuroleptic (no date) triazaspirodecanes I (R = p-FC6H4, 2-thienyl; X = O, OCH2CH2O) were prepared by alkylating the triazaspirodecano with RCX(CH2)3Cl.

AN 1975-43484 CAPLUS

DN 82-43484

TI Substituted 1,3,8-triazaspiro[4.5]decanes

IN Scharpf, William G.

PA FMC Corp.

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

FAN CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 3839340 A 19741001 US 1968-763417 19680927

PRAI US 1968-763417 19680927

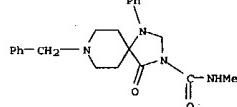
IT 54286-34-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(debenzylation of)

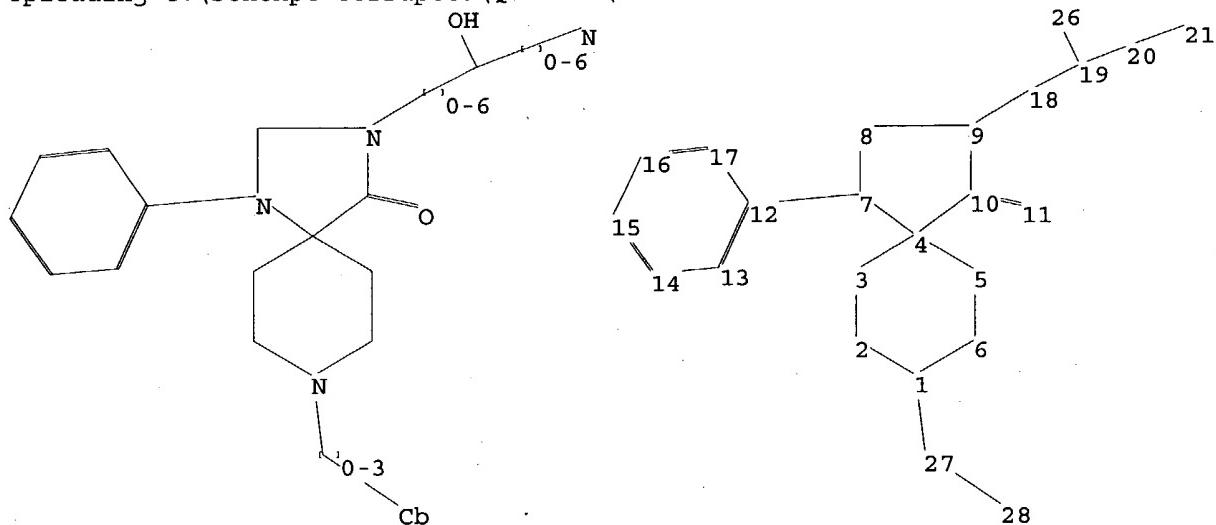
RN 54286-34-9 CAPLUS

CN 1,3,8-Triazaspiro[4.5]decane-3-carboxamide, N-methyl-4-oxo-1-phenyl-8-(phenylmethyl)- (9CI) (CA INDEX NAME)



7/15/04

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ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17
chain bonds :
1-27 7-12 9-18 10-11 18-19 19-20 19-26 20-21 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 4-10 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
exact/norm bonds :
1-2 1-6 1-27 2-3 3-4 4-5 4-7 4-10 5-6 7-8 7-12 8-9 9-10 9-18 10-11
19-26 20-21
exact bonds :
18-19 19-20 27-28
normalized bonds :
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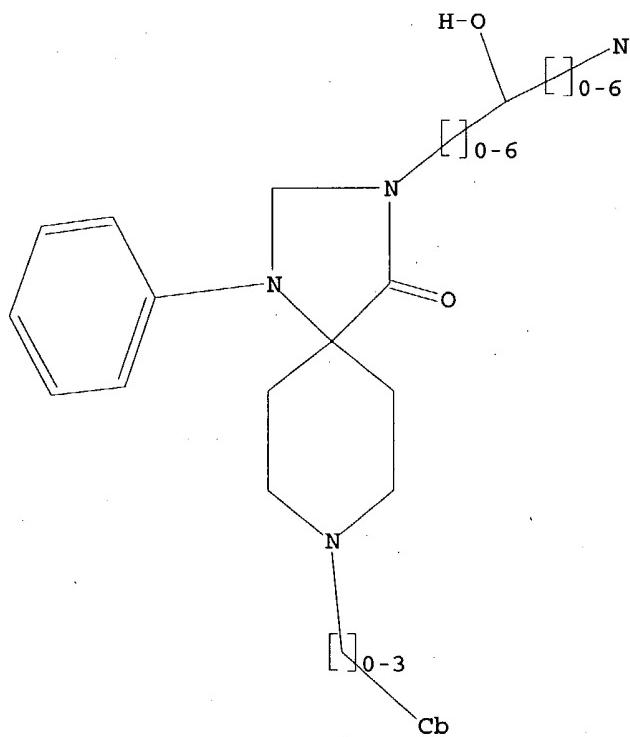
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11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 26:CLASS 27:CLASS 28:Atom

L5 STRUCTURE UPLOADED

=> d 11
L1 HAS NO ANSWERS
L1 STR

10656934

7/15/04



Structure attributes must be viewed using STN Express query preparation.

=> s 11
REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 15:05:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 33 TO ITERATE

100.0% PROCESSED 33 ITERATIONS 20 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 316 TO 1004
PROJECTED ANSWERS: 132 TO 668

L6

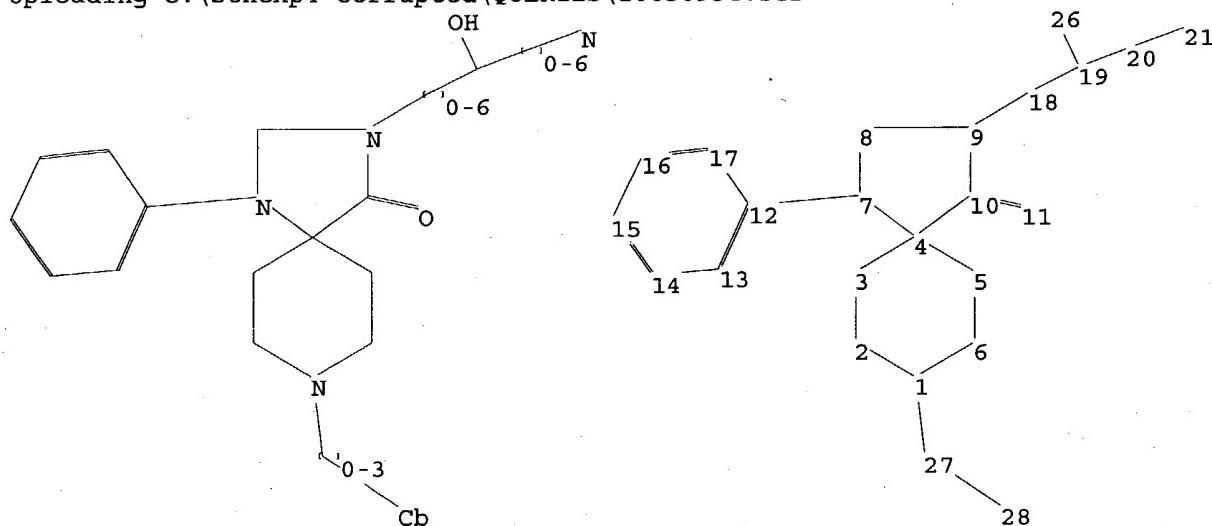
20 SEA SSS SAM L1

10656934

7/15/04

L7 5 L6

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chain nodes :
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ring nodes :
1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17
chain bonds :
1-27 7-12 9-18 10-11 18-19 19-20 19-26 20-21 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 4-10 5-6 7-8 8-9 9-10 12-13 12-17 13-14 14-15
15-16 16-17
exact/norm bonds :
1-2 1-6 1-27 2-3 3-4 4-5 4-7 4-10 5-6 7-8 7-12 8-9 9-10 9-18 10-11
19-26 20-21
exact bonds :
18-19 19-20 27-28
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

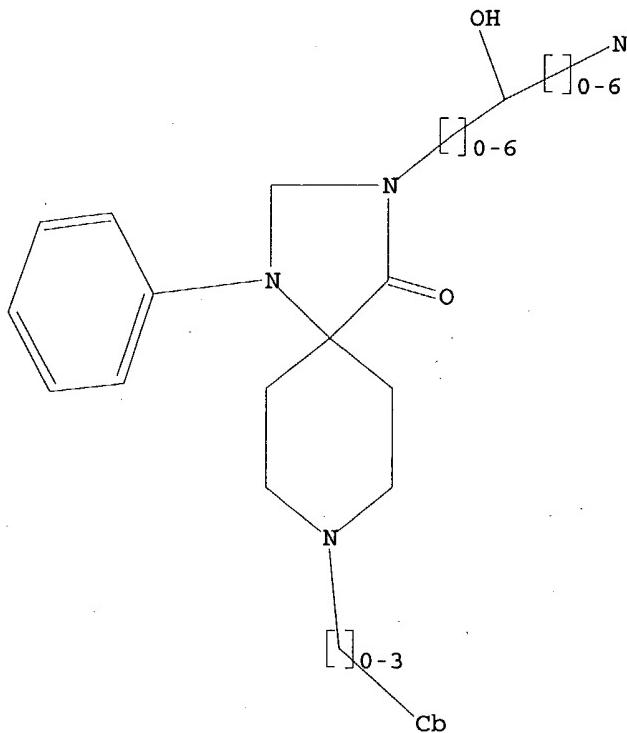
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L8 STRUCTURE UPLOADED

=> d 18
L8 HAS NO ANSWERS
L8 STR

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7/15/04



Structure attributes must be viewed using STN Express query preparation.

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REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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FULL SCREEN SEARCH COMPLETED - 875 TO ITERATE

100.0% PROCESSED 875 ITERATIONS
SEARCH TIME: 00.00.01

459 ANSWERS

L9 459 SEA SSS FUL L8

L10 13 L9

=> file uspatall
COST IN U.S. DOLLARS

| SINCE FILE
ENTRY | TOTAL
SESSION |
|---------------------|------------------|
|---------------------|------------------|

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7/15/04

| | | |
|--|------------------|---------------|
| FULL ESTIMATED COST | 0.46 | 382.76 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -9.56 |

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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 15:06:39 ON 15 JUL 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> s 19
L11 13 L9

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The saved name for a query (or structure or screen set) must end with '/Q'. The saved name for an answer set must end with '/A'. The saved name for an L# list must end with '/L'. SDI request names must end with '/S'. To see a list of all saved query, answer set,, and L# list names for this loginid, enter "DISPLAY SAVED" at an arrow prompt (=>). Enter "DISPLAY SAVED/S" to see a list of SDI request names. Enter "DISPLAY SAVED/B" to see a list of BATCH search requests.

=> s 19 <09/09/2002
NUMERIC EXPRESSION NOT VALID 'L9 <09/09/2002'
Numeric search expressions contain an operator (=>, <, =<, =>), a field qualifier, and the number or a range to be searched. Examples of valid expressions are 'LD>6', '260-280/MW', and '10 < LD < 30'. For a list of field codes in the current file, enter "HELP SFIELDS" at an arrow prompt (=>). For more information on searching in numeric fields, enter "HELP NUMERIC".

=> s 19 and <09/09/2002
MISSING TERM 'AND <09/09/2002'
The search profile that was entered contains a logical operator followed immediately by another operator.

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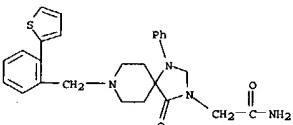
7/15/04

L13 ANSWER 1 OF 11 USPATFULL on STN
 AB The present invention relates to the method of treating cough with ORL-1 agonists, alone or in combination with additional agents for treating symptoms of cough, allergy or asthma, pharmaceutical compositions comprising the combinations, and to compounds of the formula ##STR1## or a pharmaceutically acceptable salt or solvate thereof, wherein: the dotted line represents an optional double bond; X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl or heterocycloalkyl; X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl; or X.sup.1 is optionally substituted benzofused heterocyclyl and X.sup.2 is hydrogen; or X.sup.1 and X.sup.2 together form an optionally benzofused spiro heterocycl group R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3) or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3 carbon atoms; Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl or heterocycloalkyl, or --CO.sub.2(alkyl or substituted amino) or CN; Z.sup.2 is H or Z.sup.1; Z.sup.3 is H or alkyl; or Z.sup.1, Z.sup.2 and Z.sup.3, together with the carbon to which they are attached, form bicyclic saturated or unsaturated rings; pharmaceutical compositions therefore, and the use of said compounds as nociceptin receptor inhibitors useful in the treatment of pain, anxiety, cough, asthma, depression and alcohol abuse.

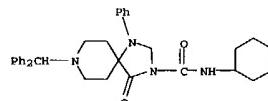
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2004:88973 USPATFULL
 TI High affinity ligands for nociceptin receptor ORL-1
 IN Tulshian, Deen, Lebanon, NJ, UNITED STATES
 Ho, Ginny D., Murray Hill, NJ, UNITED STATES
 Silverman, Lisa S., Edison, NJ, UNITED STATES
 Matasi, Julius J., Scotch Plains, NJ, UNITED STATES
 McLeod, Robbie L., Branchburg, NJ, UNITED STATES
 Hey, John A., Bloomfield, NJ, UNITED STATES
 Chapman, Richard W., Somerville, NJ, UNITED STATES
 Bercovici, Ana, West Orange, NJ, UNITED STATES
 Cuse, Francis M., Basking Ridge, NJ, UNITED STATES
 PA Schering-Plough Corporation (U.S. corporation)
 PI US 2004067950 A1 20040408
 AI US 2003-464580 A1 20030617 (10)
 RLI Continuation of Ser. No. US 2000-491780, filed on 26 Jan 2000, PENDING
 Continuation-in-part of Ser. No. US 1999-359771, filed on 26 Jul 1999.

L13 ANSWER 2 OF 11 USPATFULL on STN
 AB The present invention is directed to novel 1,3,8-triaza[4.5]decan-4-one derivatives of the general formula ##STR1## wherein all variables are as defined herein, useful in the treatment of disorders and conditions mediated by the ORL-1 G-protein coupled receptor. More particularly, the compounds of the present invention are useful in the treatment of disorders and conditions such as anxiety, depression, substance abuse, neuropathic pain, acute pain, migraine, asthma, cough and for improved cognition.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2003:159924 USPATFULL
 TI 1,3,8-Triaaza[4.5]decan-4-one derivatives useful for the treatment of ORL-1 receptor mediated disorders
 IN Jordan, Alfonzo, North Wales, PA, UNITED STATES
 Reitz, Allen B., Lansdale, PA, UNITED STATES
 Pan, Kevin, Shanghai, CHINA
 PI US 2003109539 A1 20030612
 AI US 2002-117674 A1 20020405 (10)
 PRAI US 2001-282722P 20010410 (60)
 DT Utility
 FS APPLICATION
 LREP Philip S. Johnson, Esq., Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ, 08933-7003
 CLMN Number of Claims: 17
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 2725
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 IT 473528-08-4P, 4-Oxo-1-phenyl-8-[(2-(2-thienyl)phenyl)methyl]-1,3,8-triaza[4.5]decan-3-acetamide
 (drug candidate; preparation of triazaspirodecanone derivs. for treatment of ORL-1 receptor-mediated disorders)
 RN 473528-08-4 USPATFULL
 CN 1,3,8-Triaaza[4.5]decan-3-acetamide, 4-oxo-1-phenyl-8-[(2-(2-thienyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L13 ANSWER 1 OF 11 USPATFULL on STN (Continued)
 GRANTED, Pat. No. US 6262066
 PRAI US 1998-94240P 19980727 (60)
 DT Utility
 FS APPLICATION
 LREP LERNER, DAVID, LITTENBERG, KRUMHOLZ & MENTLIK, 600 SOUTH AVENUE WEST, WESTFIELD, NJ, 07090
 CLMN Number of Claims: 19
 ECL Exemplary Claim: 1
 DRWN 4 Drawing Page(s)
 LN.CNT 3099
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 IT 256940-47-3P
 (preparation of substituted piperidines as nociceptin receptor ORL-1 agonists for use in treating cough)
 RN 256940-47-3 USPATFULL
 CN 1,3,8-Triaaza[4.5]decan-3-carboxamide, N-cyclohexyl-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L13 ANSWER 3 OF 11 USPATFULL on STN
 AB Novel compounds of the formula ##STR1## or a pharmaceutically acceptable salt or solvate thereof, wherein: the dotted line represents an optional double bond; X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl or heterocycloalkyl; X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl; or X.sup.1 is optionally substituted benzofused heterocyclyl and X.sup.2 is hydrogen; or X.sup.1 and X.sup.2 together form an optionally benzofused spiro heterocycl group R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3) or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3 carbon atoms; Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl or heterocycloalkyl, or --CO.sub.2(alkyl or substituted amino) or CN; Z.sup.2 is H or Z.sup.1; Z.sup.3 is H or alkyl; or Z.sup.1, Z.sup.2 and Z.sup.3, together with the carbon to which they are attached, form bicyclic saturated or unsaturated rings; pharmaceutical compositions therefore, and the use of said compounds as nociceptin receptor inhibitors useful in the treatment of pain, anxiety, cough, asthma, depression and alcohol abuse are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2003:106778 USPATFULL
 TI High affinity ligands for nociceptin receptor ORL-1
 IN Tulshian, Deen, Lebanon, NJ, UNITED STATES
 Ho, Ginny D., Murray Hill, NJ, UNITED STATES
 Silverman, Lisa S., Edison, NJ, UNITED STATES
 Matasi, Julius J., Scotch Plains, NJ, UNITED STATES
 McLeod, Robbie L., Branchburg, NJ, UNITED STATES
 Hey, John A., Nutley, NJ, UNITED STATES
 Chapman, Richard W., Somerville, NJ, UNITED STATES
 Bercovici, Ana, West Orange, NJ, UNITED STATES
 Cuse, Francis M., Basking Ridge, NJ, UNITED STATES
 PI US 2003073690 A1 20030417
 US 6716846 B2 20040406
 AI US 2002-155277 A1 20020523 (10)
 RLI Division of Ser. No. US 2001-769824, filed on 25 Jan 2001, PENDING
 Division of Ser. No. US 1999-359771, filed on 26 Jul 1999, GRANTED.
 Pat.
 No. US 6262066
 PRAI US 1998-94240P 19980727 (60)
 DT Utility
 FS APPLICATION
 LREP SCHERING-PLUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000 GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
 CLMN Number of Claims: 18

10656934

7/15/04

L13 ANSWER 3 OF 11 USPATFULL ON STN (Continued)

ECL Exemplary Claim: 1

DRWN 4 Drawing Page(s)

LN.CNT 2248

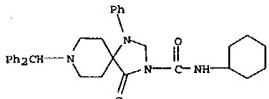
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 256940-47-3P

(preparation of substituted piperidines as nociceptin receptor ORL-1 agonists for use in treating cough)

RN 256940-47-3 USPATFULL

CN 1,3,8-Triazaaspiro[4.5]decane-3-carboxamide, N-(cyclohexyl)-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L13 ANSWER 4 OF 11 USPATFULL ON STN (Continued)

Hoffmann, Torsten, Weil am Rhein, GERMANY, FEDERAL REPUBLIC OF
Kolczewski, Sabine, Loerrach, GERMANY, FEDERAL REPUBLIC OF
Roever, Stephan, Inzlingen, GERMANY, FEDERAL REPUBLIC OF

PI US 2002006932 A1 20020117
US 6482829 B2 20021119

AI US 2001-861795 A1 20010521 (9)

PRAI EP 2000-112285 20000608

DT Utility

FS APPLICATION

LREP HOFFMANN-LA ROCHE INC., PATENT LAW DEPARTMENT, 340 KINGSLAND STREET,
NUTLEY, NJ, 07110

CLMN Number of Claims: 212

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3197

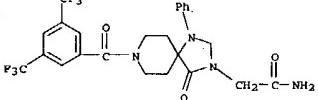
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 380198-55-0P

(drug; synthesis and use of triazaaspirodecanone derivs. as neurokinin receptor antagonists)

RN 380198-55-0 USPATFULL

CN 1,3,8-Triazaaspiro[4.5]decane-3-acetamide, 8-[3,5-bis(trifluoromethyl)benzoyl]-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



10656934

L13 ANSWER 4 OF 11 USPATFULL ON STN

AB The invention relates to compounds of the formula ##STR1##

wherein

R.sup.1 is hydrogen, lower alkyl, lower alkenyl, phenyl or the following groups --(CH₂.sub.2).sub.m-non aromatic heterocyclyl, which is optionally substituted by lower alkyl, or is --(CH₂.sub.2).sub.m-heteroaryl, which is optionally substituted by one or two substituents selected from the group consisting of lower alkyl, lower alkoxy, halogen, CF₃.sub.3, benzyl or cyano, or is --(CH₂.sub.2).sub.m-C(O)--NRR', --(CH₂.sub.2).sub.m-C(O)-lower alkyl, --(CH₂.sub.2).sub.m-O-lower alkyl, --(CH₂.sub.2).sub.m--CH(C(O)--O-lower alkyl).sub.2, --(CH₂.sub.2).sub.mCH(OH)--CH₂.sub.2-O-phenyl, --(CH₂.sub.2).sub.m--CH(CP₂).sub.3OH, --(CH₂.sub.2).sub.m-OH, --(CH₂.sub.2).sub.m-CN, --(CH₂.sub.2).sub.m-NRR', --(CH₂.sub.2).sub.m-cycloalkyl or --(CH₂.sub.2).sub.m-OHCF₂.sub.2;

R.sup.2 is hydrogen, lower alkyl, halogen or lower alkoxy;

R.sup.3 is lower alkyl, lower alkoxy, halogen or CF₃.sub.3;

R,R' are the same or different and are hydrogen or lower alkyl;

X is >N--, >C.dbd. or >CH--;

X.sup.1/X.sup.2 are independently from each other hydrogen, hydroxy or lower alkoxy or may be together an oxo group;

Y.sup.1/Y.sup.2 are independently from each other hydrogen, lower alkyl, --CH₂.sub.2).sub.m-phenyl or may be together an oxo group;

Z is a bond, --CH₂.sub.2-- or --C(O)--;

m is 0, 1, 2, 3 or 4;

n is 2 or 3;

p is 0, 1 or 2;

and pharmaceutically acceptable acid addition salts thereof. The described compounds have a good affinity to the NK1 receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 2002:12551 USPATFULL

TI Substituted heterocyclic siprodecano compound active as an antagonist of neurokinin 1 receptor

IN Galley, Guido, Rheinfelden, GERMANY, FEDERAL REPUBLIC OF
Godel, Thierry, Basle, SWITZERLAND
Goergler, Annick, Colmar, FRANCE

L13 ANSWER 5 OF 11 USPATFULL ON STN (Continued)

AB The present invention relates to the use of small organic compounds acting as opioid receptor ligands for the treatment of vasoconstrictive disturbances. In particular the present invention relates to the use of triaza-spiro compounds of formula ##STR1##

wherein

R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, z and n are defined in the specification, for the treatment of migraine, non-insulin dependent diabetes mellitus (type II diabetes), sepsis, inflammation, incontinence and/or vasoconstrictive disturbances, in particular the peripheral vasoconstrictive effects known as hot flushes or hot flashes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 2001:136792 USPATFULL

TI 1,3,8-triazaaspiro[4.5]decanones with high affinity for opioid receptor subtypes

IN Hohlweg, Rolf, Kvistgaard, Denmark

Watson, Brett, Vaerlose, Denmark

Thomsen, Christain, Stroby, Denmark

PA Novo Nordisk A/S, Bagvaerd, Denmark (non-U.S. corporation)

PI US 6277991 B1 20010821

AI US 1999-311469 19990513 (9)

PRAI DK 1998-711 19980520

DK 1998-729 19980526

DK 1998-681 19980518

DK 1998-927 19980710

DK 1999-111 19990129

US 1998-91012P 19980626 (60)

US 1998-93519P 19980721 (60)

US 1999-120295P 19990216 (60)

DT Utility

FS GRANTED

EXAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Desai, Rita

LREP Green, Esq., Reza, Gregg, Esq., Valeta A.

CLMN Number of Claims: 38

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2005

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 250686-42-1P

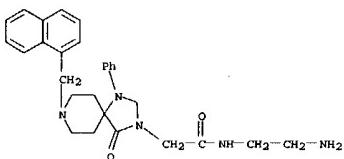
(preparation of 1,3,8-triazaaspiro[4.5]decanones and their affinity for opioid receptor subtypes)

RN 250686-42-1 USPATFULL

CN 1,3,8-Triazaaspiro[4.5]decan-3-acetamide, N-(2-aminoethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)

7/15/04

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

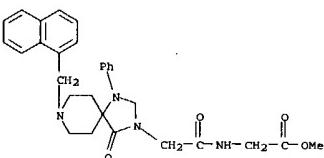


• 2 HCl

IT 250685-86-0P 250685-87-1P 250685-88-2P
 250685-89-3P 250685-90-6P 250685-91-7P
 250685-92-8P 250685-93-9P 250685-94-0P
 250685-95-1P 250685-96-2P 250685-97-3P
 250685-98-4P 250685-99-5P 250686-00-1P
 250686-01-2P 250686-02-3P 250686-03-4P
 250686-04-5P 250686-05-6P 250686-06-7P
 250686-07-8P 250686-08-9P 250686-09-0P
 250686-10-1P 250686-11-2P 250686-12-3P
 250686-13-4P 250686-14-5P 250686-15-6P
 250686-16-7P 250686-17-8P 250686-18-1P
 250686-19-2P 250686-20-3P 250686-21-4P
 250686-22-5P 250686-23-6P 250686-24-7P
 250686-25-8P 250686-26-9P 250686-27-0P
 250686-28-1P 250686-29-2P 250686-30-3P
 250686-31-4P 250686-43-2P
 250686-44-3P 250686-45-4P 250686-46-5P
 250686-47-6P 250686-48-7P 250686-49-8P
 (preparation of 1,3,8-triazaaspiro[4.5]decanones and their affinity for opioid receptor subtypes)

RN 250685-86-0 USPATFULL

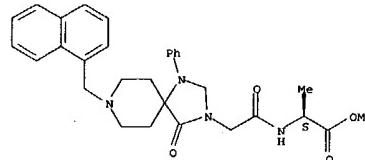
CN Glycine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)



L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

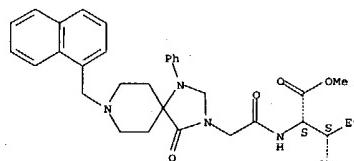
RN 250685-87-1 USPATFULL
 CN L-Alanine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250685-88-2 USPATFULL
 CN L-Isoleucine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

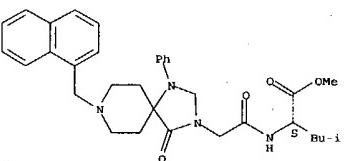
Absolute stereochemistry.



RN 250685-89-3 USPATFULL
 CN L-Leucine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

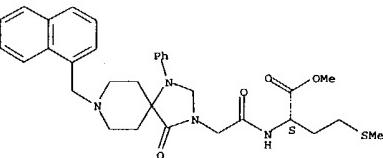
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250685-90-6 USPATFULL

CN L-Methionine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

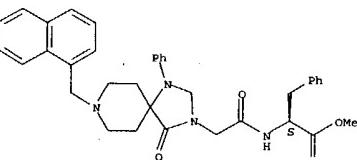
Absolute stereochemistry.



RN 250685-91-7 USPATFULL

CN L-Phenylalanine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

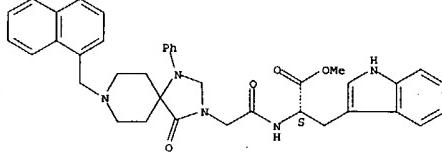


RN 250685-92-8 USPATFULL

CN L-Tryptophan, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

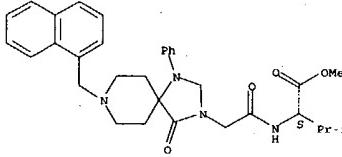
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250685-93-9 USPATFULL

CN L-Valine, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

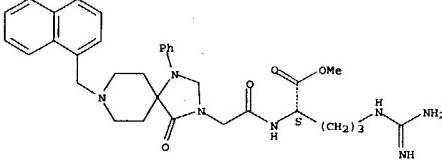
Absolute stereochemistry.



RN 250685-94-0 USPATFULL

CN L-Arginine, N2-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



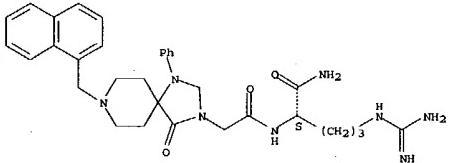
RN 250685-95-1 USPATFULL

CN 1,3,8-Triaazaaspiro[4.5]decane-3-acetamide, N-[(1S)-1-(aminocarbonyl)-4-(aminoiminoethyl)aminobutyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaaspiro[4.5]dec-3-yl]acetyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

7/15/04

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

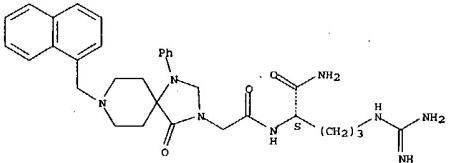


RN 250685-96-2 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-1-(aminocarbonyl)-4-((aminoiminomethyl)amino)butyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250685-95-1
CMF C32 H40 N8 O3

Absolute stereochemistry.



CM 2

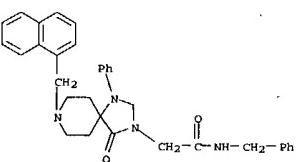
CRN 76-05-1
CMF C2 H F3 O2



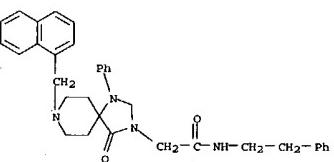
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250685-99-5 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 250686-00-1 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)

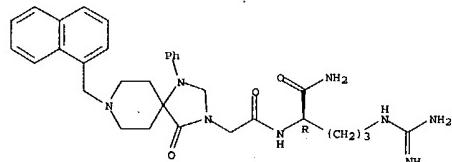


RN 250686-01-2 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
N-[3-(4-morpholinyl)propyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

RN 250685-97-3 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1R)-1-(aminocarbonyl)-4-((aminoiminomethyl)amino)butyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



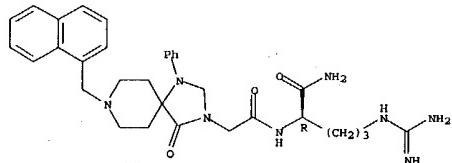
RN 250685-98-4 USPATFULL

CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1R)-1-(aminocarbonyl)-4-((aminoiminomethyl)amino)butyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250685-97-3
CMF C32 H40 N8 O3

Absolute stereochemistry.

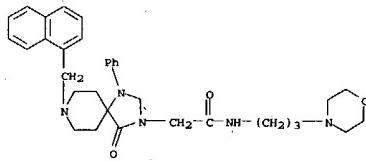


CM 2

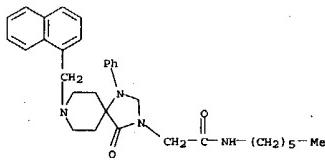
CRN 76-05-1
CMF C2 H F3 O2

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

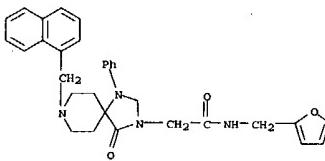
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-02-3 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
N-hexyl-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



RN 250686-03-4 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(2-furanyl methyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

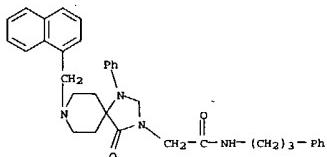


RN 250686-04-5 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-(3-phenylpropyl)- (9CI) (CA INDEX NAME)

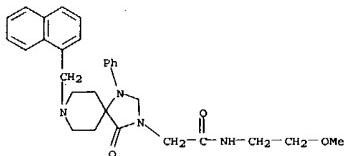
10656934

7/15/04

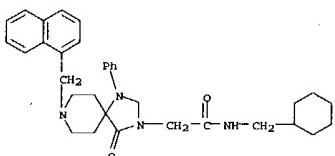
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-05-6 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(2-methoxyethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

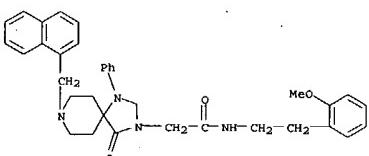


RN 250686-06-7 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(cyclohexylmethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

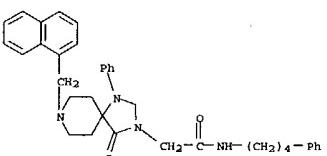


RN 250686-07-8 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(4-methoxyphenyl)methyl-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

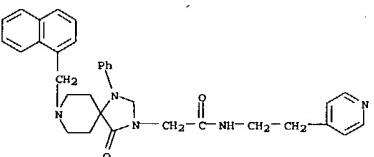
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-11-4 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-(4-phenylbutyl)- (9CI) (CA INDEX NAME)

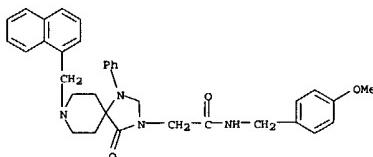


RN 250686-12-5 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-(2-(4-pyridinyl)ethyl)- (9CI) (CA INDEX NAME)

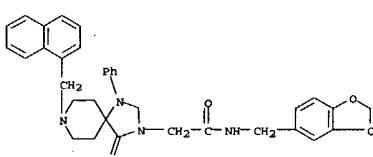


RN 250686-13-6 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[2-(4-methoxyphenyl)ethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

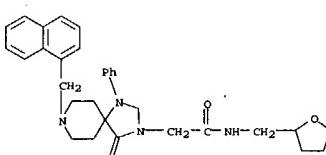
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-08-9 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(1,3-benzodioxol-5-ylmethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

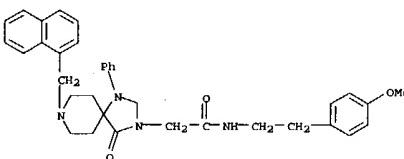


RN 250686-09-0 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)

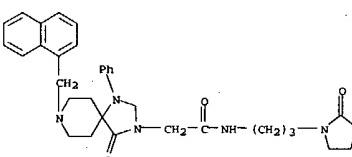


RN 250686-10-3 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(2-(2-methoxyphenyl)ethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

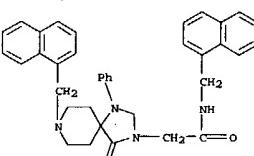
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-14-7 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-(1-naphthalenylmethyl)-4-oxo-N-[3-(2-oxo-1-pyrrolidinyl)propyl]-1-phenyl- (9CI) (CA INDEX NAME)



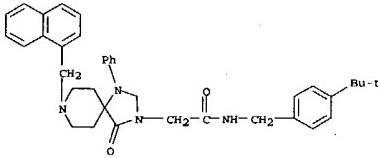
RN 250686-15-8 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N,8-bis(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



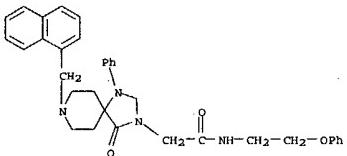
RN 250686-16-9 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(4-(1,1-dimethylethyl)phenyl)methyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

7/15/04

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

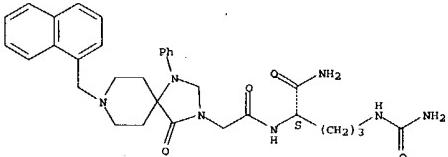


RN 250686-17-0 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
N-[(1S)-1-(aminocarbonyl)butyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



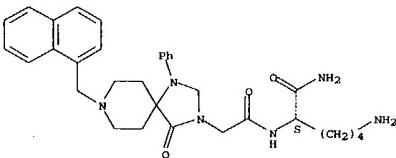
RN 250686-18-1 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-1-(aminocarbonyl)butyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



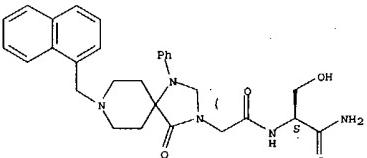
RN 250686-19-2 USPATFULL
CN Pentanediamide, 2-[[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl]-1,3,8-

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



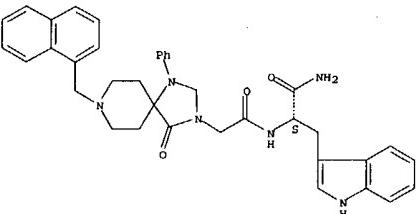
RN 250686-23-8 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-2-amino-1-(hydroxymethyl)-2-oxoethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



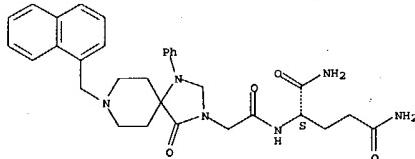
RN 250686-24-9 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-2-amino-1-(1H-indol-3-ylmethyl)-2-oxoethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



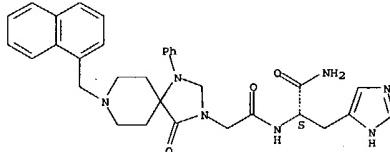
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)
triazaspiro[4.5]dec-3-yl)acetylaminol-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250686-20-5 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide,
N-[(1S)-2-amino-1-(1H-imidazol-4-ylmethyl)-2-oxoethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



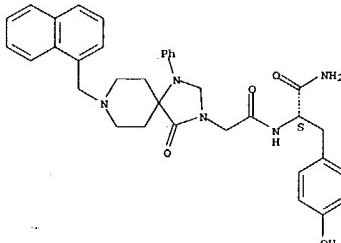
RN 250686-21-6 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-5-amino-1-(aminocarbonyl)pentyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

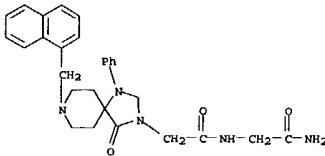
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

RN 250686-25-0 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-2-amino-1-[(4-hydroxyphenyl)methyl]-2-oxoethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250686-26-1 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-2-amino-1-[(4-hydroxyphenyl)methyl]-2-oxoethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

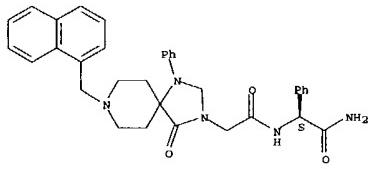


RN 250686-27-2 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-[(1S)-2-amino-2-oxo-1-phenylethyl]-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

7/15/04

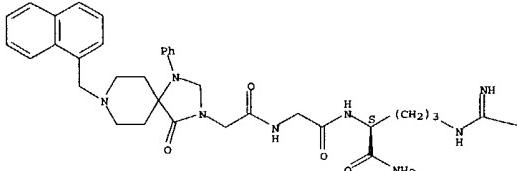
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-29-3 USPATFULL
CN L-Argininamide, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-3-yl]acetylglycyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



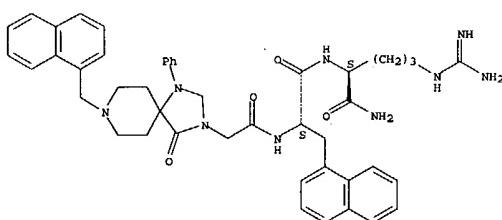
PAGE 1-B

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

RN 250686-30-7 USPATFULL
CN L-Argininamide, 3-(1-naphthalenyl)-N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-3-yl]acetyl-L-alanyl (9CI) (CA INDEX NAME)

INDEX NAME

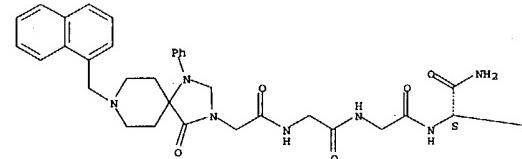
Absolute stereochemistry.



RN 250686-31-8 USPATFULL
CN L-Argininamide, N-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-3-yl]acetylglycylglycyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

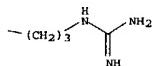
PAGE 1-A



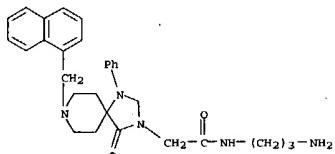
→NH₂

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

PAGE 1-B



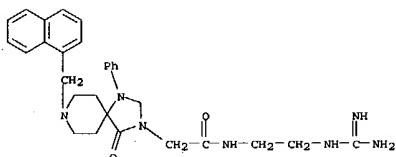
RN 250686-43-2 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(3-aminopropyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 250686-44-3 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, N-(2-[(aminoiminomethyl)amino]ethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)

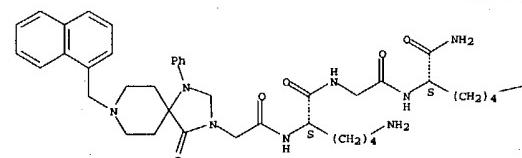


● HCl

RN 250686-45-4 USPATFULL
CN L-Lysinamide, N2-[8-(1-naphthalenylmethyl)-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-3-yl]acetyl-L-lysylglycyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

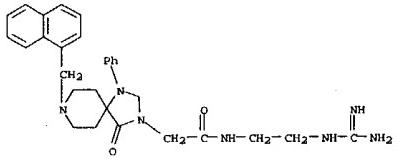


PAGE 1-B

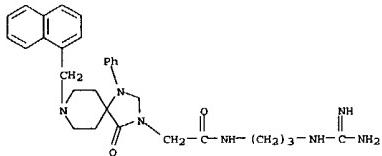
10656934

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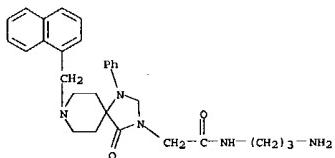
L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



RN 250686-47-6 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, N-[3-((aminoiminomethyl)aminopropyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



RN 250686-48-7 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, N-(3-aminopropyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



RN 250686-49-8 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decan-3-acetamide, N-(2-aminoethyl)-8-(1-naphthalenylmethyl)-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)

L13 ANSWER 6 OF 11 USPATFULL on STN
AB Novel compounds of the formula ##STR1##

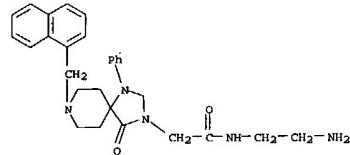
or a pharmaceutically acceptable salt or solvate thereof, wherein:
the dotted line represents an optional double bond;
X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl
or heterocycloalkyl;
X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl;
or X.sup.1 is optionally substituted benzofused heterocyclyl and
X.sup.2 is hydrogen;
or X.sup.1 and X.sup.2 together form an optionally benzofused spiro
heterocyclyl group
R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or
(R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3)
or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3
carbon atoms;
Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl
or heterocycloalkyl, or --CO sub.2(alkyl or substituted amino) or CN;
Z.sup.2 is H or Z.sup.1; Z.sup.3 is H or alkyl; or Z.sup.1, Z.sup.2 and
Z.sup.3, together with the carbon to which they are attached, form
bicyclic saturated or unsaturated rings; pharmaceutical compositions
therefore, and the use of said compounds as nociceptin receptor
inhibitors useful in the treatment of pain, anxiety, cough, asthma,
depression and alcohol abuse are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

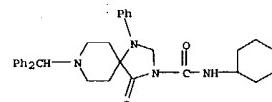
AN 2001123584 USPATFULL
TI High affinity ligands for nociceptin receptor ORL-1
IN Tuohimaa, Deen, Lebanon, NJ, United States
Ho, Ginny D., Murray Hill, NJ, United States
Silverman, Lisa S., Edison, NJ, United States
Matsai, Julius J., Scotch Plains, NJ, United States
McLeod, Robbie L., Branchburg, NJ, United States
Hey, John A., Nutley, NJ, United States
Chapman, Richard W., Somerville, NJ, United States
Bercovici, Ana, West Orange, NJ, United States
Cuss, Francis M., Basking Ridge, NJ, United States
PI US 2001011092 A1 20010802
US 6455527 B2 20020924
AI US 2001-769824 A1 20010125 (9)
RLI Division of Ser. No. US 1999-359771, filed on 26 Jul 1999, PENDING
PRAI US 1998-94240P 19980727 (60) <--
DT Utility
FS APPLICATION
LREP SCHERING-PLOUGH CORPORATION, PATENT DEPARTMENT (K-6-1, 1990), 2000
GALLOPING HILL ROAD, KENILWORTH, NJ, 07033-0530
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 2266

10656934

L13 ANSWER 5 OF 11 USPATFULL on STN (Continued)



L13 ANSWER 6 OF 11 USPATFULL on STN (Continued)
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 256940-47-3
(preparation of substituted piperidines as nociceptin receptor ORL-1
agonists for use in treating cough)
RN 256940-47-3 USPATFULL
CN 1,3,8-Triazaspiro[4.5]decan-3-carboxamide, N-cyclohexyl-8-
(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX
NAME)



● HCl

7/15/04

L13 ANSWER 7 OF 11 USPATFULL on STN
AB Novel compounds of the formula ##STR1##

or
X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl heterocycloalkyl;
X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl;
or X.sup.1 is optionally substituted benzofused heterocyclyl and
X.sup.2 is hydrogen;
or X.sup.1 and X.sup.2 together form an optionally benzofused Spiro heterocyclyl group

R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3) or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3 carbon atoms;

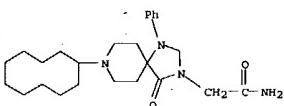
or
Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl heterocycloalkyl, or --CO--sub.2 (alkyl or substituted amino) or CN; Z.sup.2 is H or Z.sup.1; Z.sup.3 is H or alkyl; or Z.sup.1, Z.sup.2 and Z.sup.3, together with the carbon to which they are attached, form bicyclic saturated or unsaturated rings; pharmaceutical compositions therefore, and the use of said compounds as nociceptin receptor inhibitors useful in the treatment of pain, anxiety, cough, asthma, depression and alcohol abuse are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 2001112331 USPATFULL
TI High affinity ligands for nociceptin receptor ORL-1
IN Tulshiani, Deen, Lebanon, NJ, United States
Ho, Ginny D., Murray Hill, NJ, United States
Silverman, Lieb S., Edison, NJ, United States
Matasi, Julius J., Scotch Plains, NJ, United States
McLeod, Robbie L., Branchburg, NJ, United States
Hey, John A., Nutley, NJ, United States
Chapman, Richard W., Somerville, NJ, United States
Bercovici, Ana, West Orange, NJ, United States
Cuss, Francis M., Basking Ridge, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 6262066 B1 20010717
AI US 1999-359771 19990726 (9)
PRAI US 1998-94240P 19980727 (60) <--
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
LREP Magatti, Anita W.
CLMN Number of Claims: 16

L13 ANSWER 8 OF 11 USPATFULL on STN
AB The present invention relates to compounds of formula I and pharmaceutically acceptable acid addition salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AN 2000037922 USPATFULL
TI 1,3,8-triaza spiro (4,5)decan-4-on derivatives
IN Adam, Geo, Schopfheim, Germany, Federal Republic of
Csura, Andrea, Basel, Switzerland
Galley, Caido, Rheinfelden, Germany, Federal Republic of
Jenck, Fran.cedilla.ois, Riedisheim, France
Rover, Stephan, Inzlingen, Germany, Federal Republic of
Wichmann, Jurgen, Steinien, Germany, Federal Republic of
PA Hoffman-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
PI US 6043366 20000328
AI US 1998-204184 19981203 (9)
PRAI EP 1997-121427 19971205 <--
DT Utility
PS Granted
EXNAM Primary Examiner: Rotman, Alan L.; Assistant Examiner: Desai, Rita
LREP Johnston, George W., Rocha-Tramaloni, Patricia S., Ebel, Eileen M.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRW No Drawings
LN.CNT 1533
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 227028-91-3P, 2-(8-Cyclodetyl-4-oxo-1-phenyl-1,3,8-triaza spiro[4.5]decane-3-yl)acetamide hydrochloride 227028-94-6P,
N-Benzyl-2-(8-cyclodetyl-4-oxo-1-phenyl-1,3,8-triaza spiro[4.5]dec-3-yl)acetamide hydrochloride
(target compound; preparation of triazaspirodecanone derivs. as OFQ receptor agonists and antagonists)
RN 227028-91-3 USPATFULL
CN 1,3,8-Triaza spiro[4.5]decane-3-acetamide, 8-cyclodetyl-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)

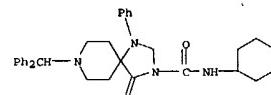


● HCl

RN 227028-94-6 USPATFULL
CN 1,3,8-Triaza spiro[4.5]decane-3-acetamide, 8-cyclodetyl-4-oxo-1-phenyl-N-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

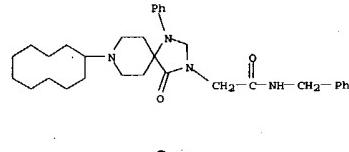
L13 ANSWER 8 OF 11 USPATFULL on STN (Continued)

ECL Exemplary Claim: 1
DRW 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2125
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 256940-47-3P
(preparation of substituted piperidines as nociceptin receptor ORL-1 agonists for use in treating cough)
RN 256940-47-3 USPATFULL
CN 1,3,8-Triaza spiro[4.5]decane-3-carboxamide, N-cyclohexyl-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L13 ANSWER 8 OF 11 USPATFULL on STN (Continued)



● HCl

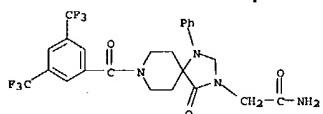
10.656934

7/15/04

L13 ANSWER 9 OF 11 USPAT2 on STN
 AB Novel compounds of the formula ##STR1##
 or a pharmaceutically acceptable salt or solvate thereof, wherein:
 the dotted line represents an optional double bond;
 X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl
 or heterocycloalkyl;
 X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl;
 or X.sup.1 is optionally substituted benzofused heterocyclyl and
 X.sup.2 is hydrogen;
 or X.sup.1 and X.sup.2 together form an optionally benzofused spiro
 heterocyclyl group
 R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or
 (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3)
 or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3
 carbon atoms;
 Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl
 or heterocycloalkyl, or --CO.sub.2(alkyl or substituted amino) or CN;
 Z.sup.2 is H or Z.sup.1; Z.sup.3 is H oralkyl; or Z.sup.1, Z.sup.2 and
 Z.sup.3, together with the carbon to which they are attached, form
 bicyclic saturated or unsaturated rings; pharmaceutical compositions
 therefore, and the use of said compounds as nociceptin receptor
 inhibitors useful in the treatment of pain, anxiety, cough, asthma,
 depression and alcohol abuse are disclosed.

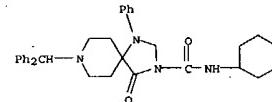
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2003-106778 USPAT2
 TI High affinity ligands for nociceptin receptor ORL-1
 IN Tulshian, Deen, Lebanon, NJ, United States
 Ho, Ginny D., Murray Hill, NJ, United States
 Silverman, Lisa S., Edison, NJ, United States
 Mataasi, Julius J., Scotch Plains, NJ, United States
 McLeod, Robbie L., Branchburg, NJ, United States
 Hey, John A., Nutley, NJ, United States
 Chapman, Richard W., Somerville, NJ, United States
 Bercovici, Ana, West Orange, NJ, United States
 Cusa, Francis M., Basking Ridge, NJ, United States
 PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
 PI US 6716846 B2 20040406
 AI US 2002-155277 20020523 (10)
 RLI Division of Ser. No. US 2001-769824, filed on 25 Jan 2001, now
 patented,
 Pat. No. US 6455527 Division of Ser. No. US 1999-359771, filed on 26
 Jul 1999, now patented, Pat. No. US 6262066
 PRAI US 1998-94240P 19980727 (60)

L13 ANSWER 10 OF 11 USPAT2 on STN
 AB The invention relates to compounds of the formula ##STR1##
 as described herein and pharmaceutically acceptable acid addition salts
 thereof. The described compounds have a good affinity to the NK1
 receptor.
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2002-12551 USPAT2
 TI Substituted heterocyclic siprodecanone compound active as an antagonist
 of neurokinin 1 receptor
 IN Galley, Guido, Rheinfelden, GERMANY, FEDERAL REPUBLIC OF
 Godel, Thierry, Basel, SWITZERLAND
 Goergler, Annick, Colmar, FRANCE
 Hoffmann, Torsten, Weil am Rhein, GERMANY, FEDERAL REPUBLIC OF
 Kolczewski, Sabine, Loerrach, GERMANY, FEDERAL REPUBLIC OF
 Roever, Stephan, Inzlingen, GERMANY, FEDERAL REPUBLIC OF
 PA Hoffmann-La Roche Inc., Nutley, NJ, United States (U.S. corporation)
 PI US 6482829 B2 20021119
 AI US 2001-861795 20010521 (9)
 PRAI EP 2000-112285 20000608
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Huang, Evelyn Mei
 LREP Johnston, George W., Rocha-Tramaloni, Patricia S., Dawson, Arthur D.
 CLMN Number of Claims: 211
 ECL Exemplary Claim: 1
 DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
 LN.CNT 3119
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 IT 380198-55-0P
 (drug; synthesis and use of triazaspirodecanone derivs. as neurokinin
 receptor antagonists)
 RN 380198-55-0 USPAT2
 CN 1,3,8-Triazaspiro[4.5]decane-3-acetamide, 8-[3,5-bis(trifluoromethyl)benzoyl]-4-oxo-1-phenyl- (9CI) (CA INDEX NAME)



L13 ANSWER 9 OF 11 USPAT2 on STN (Continued)
 AB Novel compounds of the formula ##STR1##
 or a pharmaceutically acceptable salt or solvate thereof, wherein:
 the dotted line represents an optional double bond;
 X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl
 or heterocycloalkyl;
 X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl;
 or X.sup.1 is optionally substituted benzofused heterocyclyl and
 X.sup.2 is hydrogen;
 or X.sup.1 and X.sup.2 together form an optionally benzofused spiro
 heterocyclyl group
 R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or
 (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3)
 or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3
 carbon atoms;
 Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl
 or heterocycloalkyl, or --CO.sub.2(alkyl or substituted amino) or CN;
 Z.sup.2 is H or Z.sup.1; Z.sup.3 is H oralkyl; or Z.sup.1, Z.sup.2 and
 Z.sup.3, together with the carbon to which they are attached, form
 bicyclic saturated or unsaturated rings; pharmaceutical compositions
 therefore, and the use of said compounds as nociceptin receptor
 inhibitors useful in the treatment of pain, anxiety, cough, asthma,
 depression and alcohol abuse are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 IT 256940-47-3P
 (preparation of substituted piperidines as nociceptin receptor ORL-1
 agonists for use in treating cough)
 RN 256940-47-3 USPAT2
 CN 1,3,8-Triazaspiro[4.5]decane-3-carboxamide, N-cyclohexyl-8-
 (diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (9CI) (CA INDEX
 NAME)



● HCl

L13 ANSWER 11 OF 11 USPAT2 on STN
 AB Novel compounds of the formula ##STR1##
 or a pharmaceutically acceptable salt or solvate thereof, wherein:
 the dotted line represents an optional double bond;
 X.sup.1 is optionally substituted alkyl, cycloalkyl, aryl, heteroaryl
 or heterocycloalkyl;
 X.sup.2 is --CHO, --CN, optionally substituted amino, alkyl, or aryl;
 or X.sup.1 is optionally substituted benzofused heterocyclyl and
 X.sup.2 is hydrogen;
 or X.sup.1 and X.sup.2 together form an optionally benzofused spiro
 heterocyclyl group
 R.sup.1, R.sup.2, R.sup.3 and R.sup.4 are independently H and alkyl, or
 (R.sup.1 and R.sup.4) or (R.sup.2 and R.sup.3) or (R.sup.1 and R.sup.3)
 or (R.sup.2 and R.sup.4) together can form an alkylene bridge of 1 to 3
 carbon atoms;
 Z.sup.1 is optionally substituted alkyl, aryl, heteroaryl, cycloalkyl
 or heterocycloalkyl, or --CO.sub.2(alkyl or substituted amino) or CN;
 Z.sup.2 is H or Z.sup.1; Z.sup.3 is H oralkyl; or Z.sup.1, Z.sup.2 and
 Z.sup.3, together with the carbon to which they are attached, form
 bicyclic saturated or unsaturated rings;
 pharmaceutical compositions therefore, and the use of said compounds as
 nociceptin receptor inhibitors useful in the treatment of pain,
 anxiety, cough, asthma, depression and alcohol abuse are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AN 2001-123584 USPAT2
 TI High affinity ligands for nociceptin receptor ORL-1
 IN Tulshian, Deen, Lebanon, NJ, United States
 Ho, Ginny D., Murray Hill, NJ, United States
 Silverman, Lisa S., Edison, NJ, United States
 Mataasi, Julius J., Scotch Plains, NJ, United States
 McLeod, Robbie L., Branchburg, NJ, United States
 Hey, John A., Nutley, NJ, United States
 Chapman, Richard W., Somerville, NJ, United States
 Bercovici, Ana, West Orange, NJ, United States
 Cusa, Francis M., Basking Ridge, NJ, United States
 PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
 PI US 6455527 B2 20020924
 AI US 2001-769824 20010125 (9)
 RLI Division of Ser. No. US 1999-359771, filed on 26 Jul 1999
 PRAI US 1998-94240P 19980727 (60)
 DT Utility
 FS GRANTED
 EXNAM Primary Examiner: Rao, Deepak R.
 LREP Magatti, Anita W.
 CLMN Number of Claims: 9
 ECL Exemplary Claim: 1

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L13 ANSWER 11 OF 11 USPAT2 on STN (Continued)

DRWN 4 Drawing Figure(s); 4 Drawing Page(s)

LN.CNT 1774

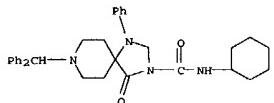
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 256940-47-3P

(preparation of substituted piperidines as nociceptin receptor ORL-1 agonists for use in treating cough)

RN 256940-47-3 USPAT2

CN 1,3,8-Triazaspiro[4.5]decane-3-carboxamide, N-cyclohexyl-8-(diphenylmethyl)-4-oxo-1-phenyl-, monohydrochloride (HCl) (CA INDEX NAME)



• HCl

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7/15/04

=> logoff Y
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 132.72 | 515.48 |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
CA SUBSCRIBER PRICE

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 0.00 | -9.56 |

STN INTERNATIONAL LOGOFF AT 15:15:00 ON 15 JUL 2004

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